REMARKS

Claims 122, 124-132, 134-147 presently appear in this case. Claims 132--141 have been withdrawn from consideration. No claims have been allowed. The official action of May 12, 2004, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to a pharmaceutical composition, in unit dosage form, which includes a pharmaceutically acceptable carrier and, as active ingredient, an *in vivo* non-propagatable particle displaying an epitope which elicits Aβ-binding antibodies when administered to a subject. The epitope is such that the antibodies inhibit aggregation of the β-amyloid in the subject. The invention is also directed to a method for treating Alzheimer's disease by administration of such a composition.

The examiner states that applicant's traversal of the restriction requirement between the composition and the methods of use thereof will not be withdrawn, because it was proper with respect to the claims as originally presented, and amending the claims after the establishment of lack of unity cannot void the restriction requirement. Nevertheless, the examiner states that if the product claims are subsequently found to be allowable, then the withdrawn method claims that depend from or otherwise include all of the limitations of the allowable product claims will be rejoined in accordance with the provisions of MPEP §821.04. The examiner states that until an elected product claim is found allowable, an

otherwise proper restriction requirement between product claims and method claims may be maintained. This lack of unity requirement is again respectfully traversed.

The examiner states that amending the claims after the establishment of lack of unity cannot void the restriction requirement. However, applicant is not aware of any Patent and Trademark Office policy to this effect. If the claims are amended so as to create unity of invention, then the restriction requirement is no longer applicable and must be withdrawn. It is never appropriate for two patents to issue on the same invention, regardless of when the claims are amended. Furthermore, in this case the claims were amended in order to create unity of invention prior to the initial examination on the merits. There is no reason why the composition and method claims in this case should not have been examined together on initial examination, as is required by 37 C.F.R. §1.475(b)(2). This regulation requires that all of the claims be examined now, and that the examination of the method claims not await allowance of the product claims. It is understood and appreciated that the examiner has agreed to rejoin the method claims if the product claims are found allowable. Nevertheless, consideration and allowance at the present time of all of the claims now present in the case is respectfully urged.

The examiner states that claim 29 is directed to an invention that is independent or distinct from the invention

elected, as it is drawn to diseases not included in the elected invention.

Claim 29 has now been deleted without prejudice to the continuation of prosecution thereof in a continuing application, thus obviating this part of the restriction requirement.

The examiner states that the disclosure is objected to because of certain specified informalities. These informalities have now been corrected. Please note that the correction of the misspelling of "deuced" at page 14, line 18, has already been corrected by applicant's preliminary amendment of August 7, 2001, which the examiner states has been received and entered in full.

The examiner states that the application contains sequence disclosures that fail to comply with the requirements of 37 C.F.R. §1.821-1.825. The examiner points out that amino acid sequences are disclosed in Fig. 5, and the examiner states that the epitope "EFRH" must be accompanied by its sequence ID number throughout the specification.

The specification has now been extensively amended in order to correct all typographical and clerical errors that have been noted, as well as to insert sequence ID numbers for the epitope "EFRH" wherever it appears, and to insert reference to sequence ID numbers in Fig. 25. Accordingly, a substitute specification accompanies this amendment, along with a copy of the specification marked up to show the differences between the substitute specification and the

originally filed specification. The substitute specification contains no new matter. Thus, it should be accepted pursuant to 37 C.F.R. §1.125(b). As no new sequences were added to the sequence listing, no changes to the sequence listing are necessary. However, the specification now fully complies with the rules.

The examiner has objected to the drawings as failing to comply with 37 C.F.R. §1.84(p)(5) because they do not include the reference signs mentioned in the description. The examiner specifically refers to the lanes that are not present in the drawing of Fig. 1. The examiner also states that Figs. 14, 15 and 17 are too dark to decipher any information contained therein.

As to Fig. 1D, the specification has now been amended so as not to refer to lanes designated "lane 1", "lane 2", etc. Instead, the description of this figure refers to the first lane, the second lane, and the third lane. As one can determine which are the first, second and third lanes without labels, no amendment to the figure is necessary in order to obviate this part of the objection.

With respect to originally filed Figs. 15 and 17, it is now proposed to delete these figures altogether, and to renumber the remaining figures accordingly. Attached hereto as Appendix D is a proposed amendment to Figs. 15-31 showing the proposed renumbering and deletions, and are marked in red. The specification has been amended to correct the numbering of all references to the figures where necessary. It is

requested that the examiner accept these corrected drawings and that they be substituted for originally appearing Figs. 15-33.

With respect to Fig. 14, attached hereto is a proposed new Fig. 14, which shows the details thereof more clearly. It is respectfully requested that this new Fig. 14 be accepted and substituted for present Fig. 14. A complete new set of drawings (Figs. 1-31) are attached hereto as Appendix C, incorporating the proposed corrections of Appendix D and presenting all of the figures in clearer form. Please substitute this new set of drawings for that originally of record. It is urged that these amendments to the drawings obviate all of the objections noted by the examiner.

Claims 28, 30 and 31 have been objected to for reciting non-elected subject matter.

These claims have now been deleted, thus obviating this objection.

Claims 27, 28, 30-39 and 122-131 have been rejected under the judicially created doctrine of obviousness type double patenting as being unpatentable over claims 1-11 of U.S. Patent no. 6,703,015, as well as being unpatentable over claims 15 and 16 of copending application no. 09/808,037, as well as being unpatentable over claims 15, 16 and 39 of copending application no. 10/384,788.

It is requested that these double patenting rejections be held in abeyance until allowable subject matter is indicated in this case, at which time a comparison can be

made to determine whether or not the claims are really obvious over one another. If so, a terminal disclaimer will be filed in order to obviate the rejection. The requirement for the filing of a terminal disclaimer is essentially a requirement as to form not necessary to further consideration of the claims, and thus can be held in abeyance in accordance with 37 C.F.R. §1.111(b).

Claims 27, 28, 30-39 and 122-131 have been rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for a pharmaceutical composition in unit dosage form comprising a pharmaceutically acceptable carrier, and, as an active ingredient, a filamentous bacteriophage displaying an epitope selected from the group consisting of EFRH, DAEFRH, DAEFRHD, DAEFRHDSG, and Aβ, which elicit Aβ-binding antibodies against said epitopes when administered to a subject, wherein said antibodies inhibit aggregation of said β-amyloid in the subject and/or cause disaggregation of β-amyloid in said subject, does not reasonably provide enablement for other display vehicles, other viruses, other epitopes, other aggregating proteins, any other plaque-related disease or prevention thereof. This rejection is respectfully traversed.

Claims 1-13 and 27-39 have now been deleted without prejudice toward continuation of prosecution thereof in a continuing application. Claim 122 has been amended to use substantially the wording that the examiner has conceded is enabled in the present specification. However, rather than

specifying "filamentous bacteriophage" as the carrier, it specifies a virus that is an "*in vivo* non-propagatable particle" as previously claimed in claim 123. Furthermore, rather than specify the specific epitopes of Aβ that were used in the examples, the claim is slightly broader in referring to the epitope as being any epitope that elicits Aβ-binding antibodies against that epitope when administered to a subject, and which antibodies inhibit aggregation of β-amyloid. All of the examiner's comments about lack of enablement for other aggregating proteins, and other plaque-related diseases or prevention are thus inapplicable to any of the presently amended claims.

As to other epitopes of Aβ, Aβ is a sufficiently short polypeptide (only 42 residues) that it would not involve undue experimentation to test each epitope thereof to see if it elicits Aβ-binding antibodies when administered to a subject, which antibodies inhibit aggregation of Aβ. There is no justification to limit applicant only to the preferred embodiments of the examples when other epitopes of Aβ can readily be tested, particularly in light of the fact that Aβ is only 42 amino acids long.

As to the carrier being a virus that is an *in vivo* non-propagatable particle, reference is made to paragraphs 44 and 131 of the substitute specification. The examiner concedes that there is enabling disclosure when the display vehicle is a filamentous bacteriophage. However, once this is established, as the examiner has conceded, the statement that

the composition would be operable if the epitope is displayed on a virus that is an *in vivo* non-propagatable particle becomes fully credible. Those of ordinary skill in the art would know how to do this, as vaccines carried on viruses that are *in vivo* non-propagatable particles are well known in the art. It would not take undue experimentation to cause the epitope, which has been proven to work using filamentous bacteriophage, to be displayed on the surface of a virus that is an *in vivo* non-propagatable particle. Claims directed to compositions where the epitope is on a filamentous bacteriophage have already been patented in the patent 6,703,015, which issued in a sister application to the present application. The burden is on the examiner to show why the display of the epitopes of the present invention on a virus that is an *in vivo* non-propagatable particle would not be expected to be operable in light of the proof that the invention works when the display vehicle is a filamentous bacteriophage. Furthermore, the examiner has not established why it would take undue experimentation to create such display vehicles displaying such epitopes, particularly in view of the fact that *in vivo* non-propagatable particles are commonly used in vaccines. Accordingly, the full breadth of amended claim 122 is supported by an enabling disclosure.

New claims 142-147 have now been added. Claims 142 and 143 have language with respect to the epitope that the examiner has conceded is enabled, and thus the present rejection as it applies to the epitope cannot apply to either

of these claims. Claim 144 is only slightly broader in stating that the epitope comprises EFRH. Claims 145-147 mimic composition claims 142-144, but are method claims. As all of the epitopes that the examiner concedes to be enabled are part of Aβ and include EFRH, there is no reason to believe that any other epitope of Aβ that includes EFRH will not also be operable.

For all of these reasons, reconsideration and withdrawal of this rejection with respect to all of the claims now present in the case are respectfully urged.

Claims 27, 28, 30-39, and 122-131 have been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey that the inventors had possession of the claimed invention. The examiner particularly refers to the terms "display vehicle", "aggregating proteins", and "epitope", particularly in view of the fact that the epitope is defined by originating from any or all of any number of aggregating proteins. This rejection is respectfully traversed.

As discussed above, claims 27, 28, 30-39, 123, have now been deleted without prejudice toward the further prosecution thereof in a continuing application. Claim 122 has been amended so as to refer only to viruses that are an *in vivo* non-propagatable particle as the display vehicle, and only to epitopes which are an epitope of β-amyloid and elicit Aβ-binding proteins against said epitope when administered to

a subject, which antibodies inhibit aggregation of Aβ. Claim 122 further specifies that the aggregating protein is Aβ. Applicants were clearly in possession of these epitopes in light of the disclosure in the specification. In light of paragraphs 44 and 131 of the specification, applicants were clearly in possession of the concept of using a virus that is an *in vivo* non-propagatable particle as the display vehicle. As the claims are no longer so broad as to read on embodiments that were allegedly not in the possession of the inventors, this rejection is no longer applicable to the amended claims. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

It is submitted that all of the claims now present in the case clearly define over the references of record and fully comply with 35 U.S.C. §112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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Attorneys for Applicant(s)

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Amendments to the Drawings:

Please replace the originally filed drawing sheets 1-25 with formal drawing sheets 1-20. Originally filed Figures 15 and 17 have been deleted. Original Figure 16 has now been renumbered as new Figure 15 and original Figures 18-33 have now been renumbered as new Figs. 16-31, respectively.

Attachment: **Appendix C** - Formal Drawings
Appendix D - Annotated Sheets 13-25 Showing Changes

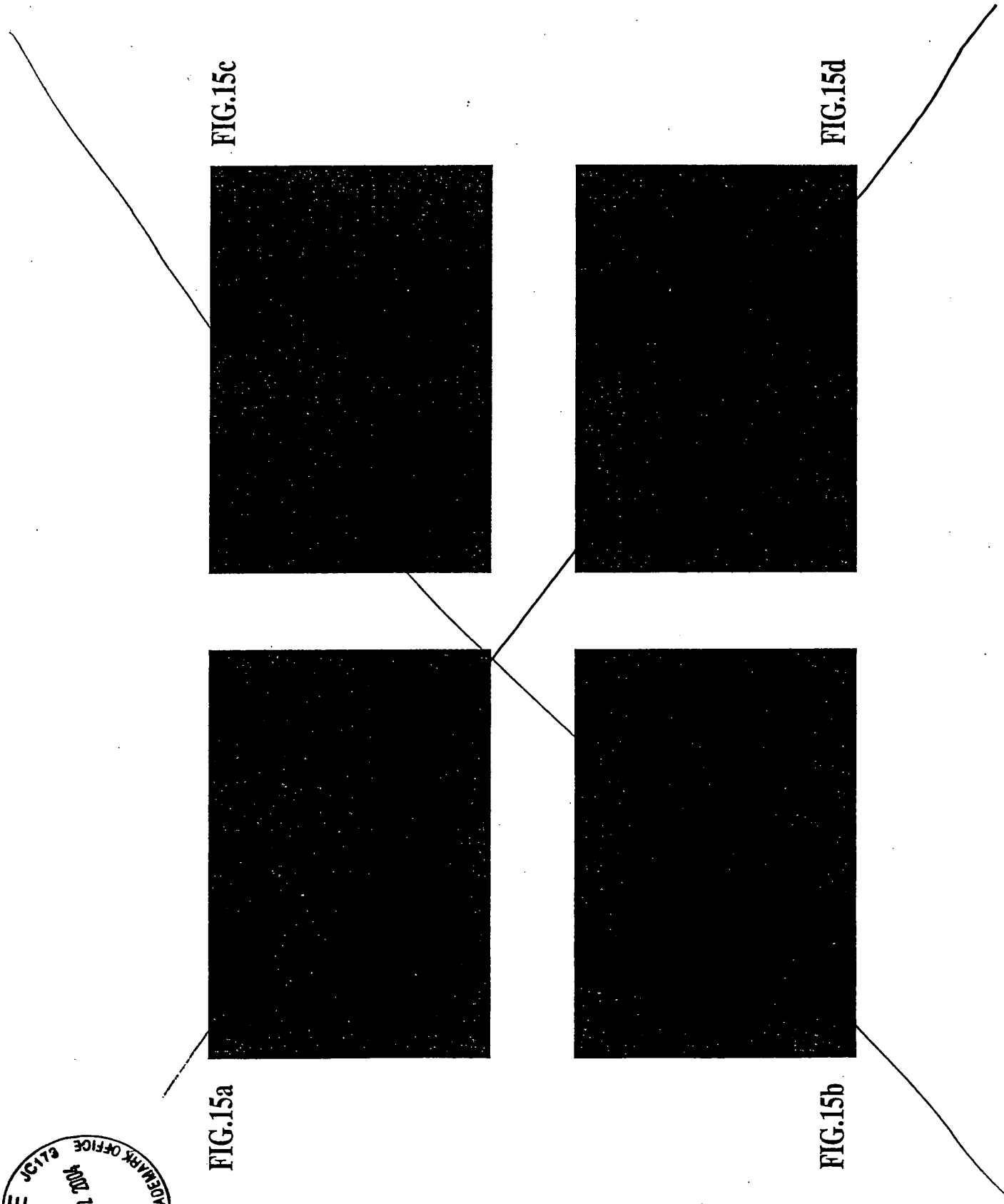


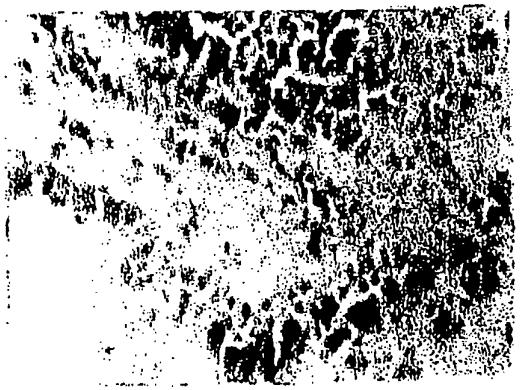
FIG.15c

FIG.15d

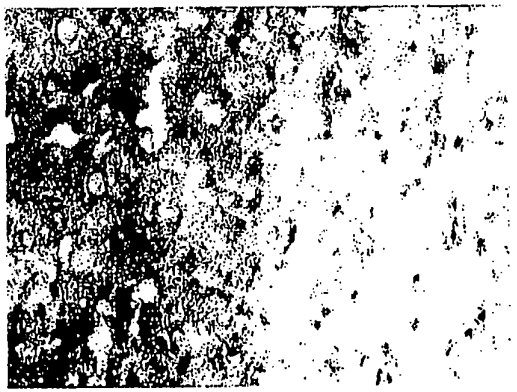
FIG.15a

FIG.15b

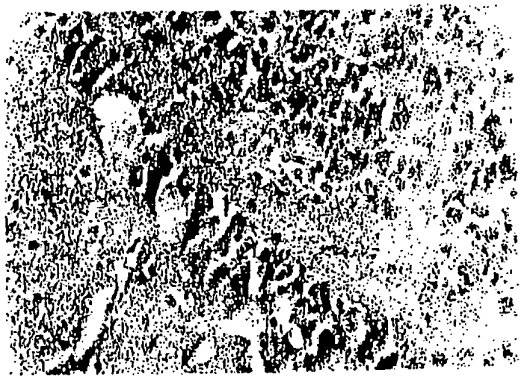
15a
FIG. ~~16a~~



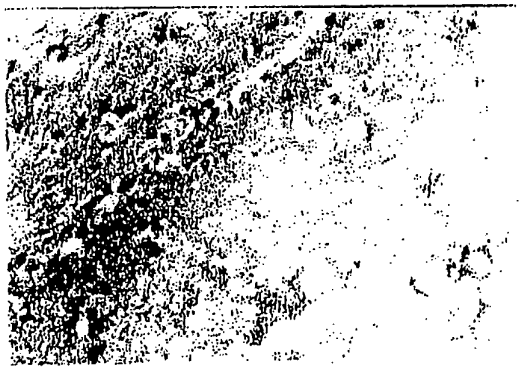
15c
FIG. ~~16c~~



15b
FIG. ~~16b~~



15d
FIG. ~~16d~~



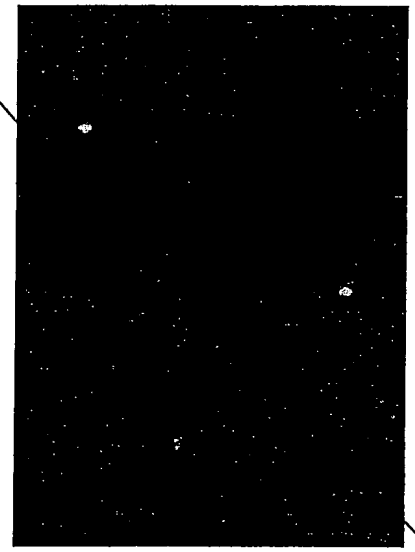


FIG.17c

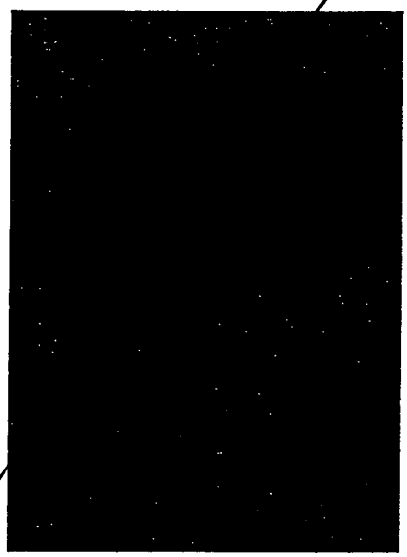


FIG.17d

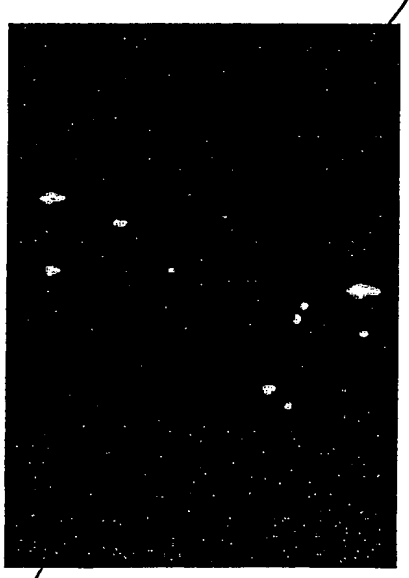


FIG.17a

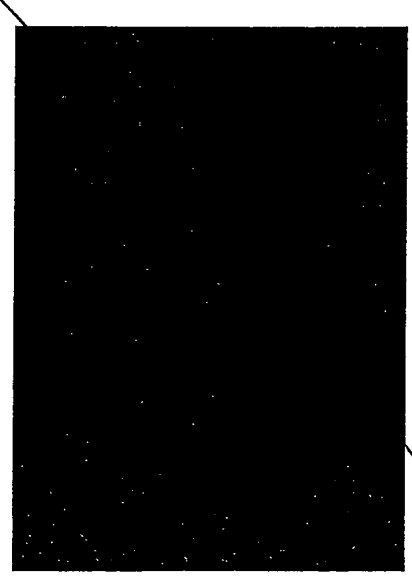


FIG.17b

Fig 16a ~~18a~~

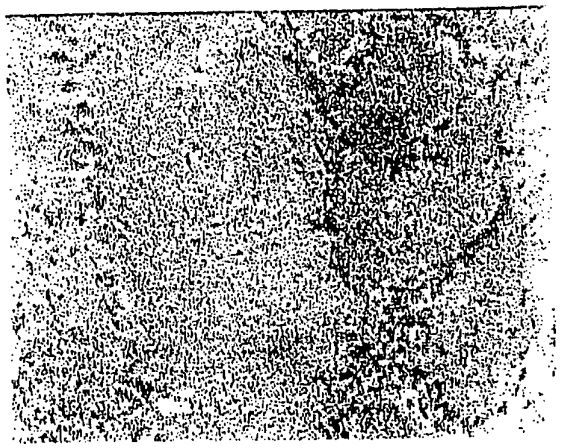


Fig ~~18c~~ 16c

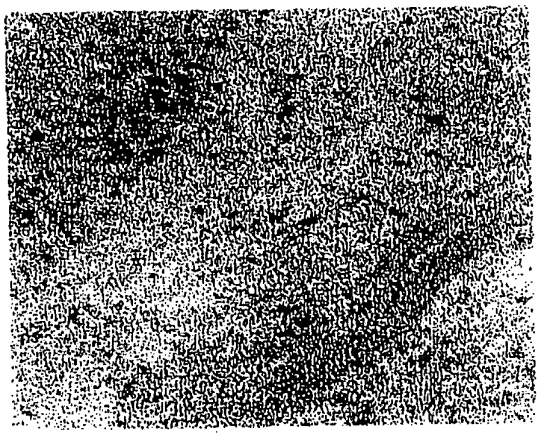


Fig 16b ~~18b~~

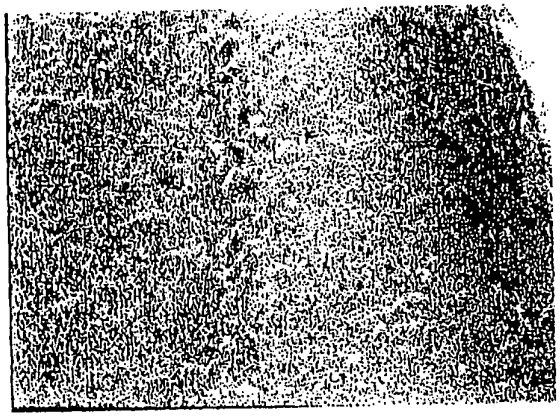
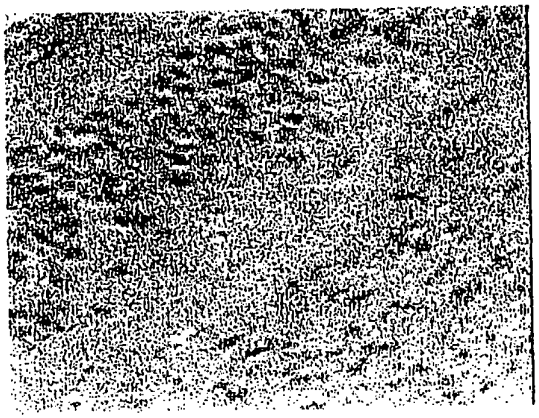
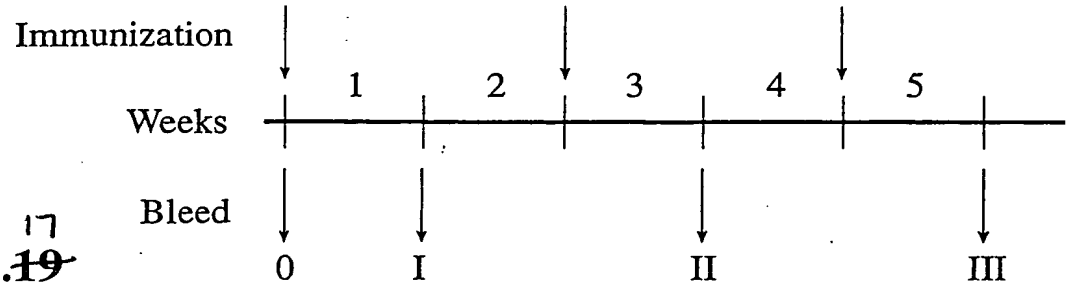
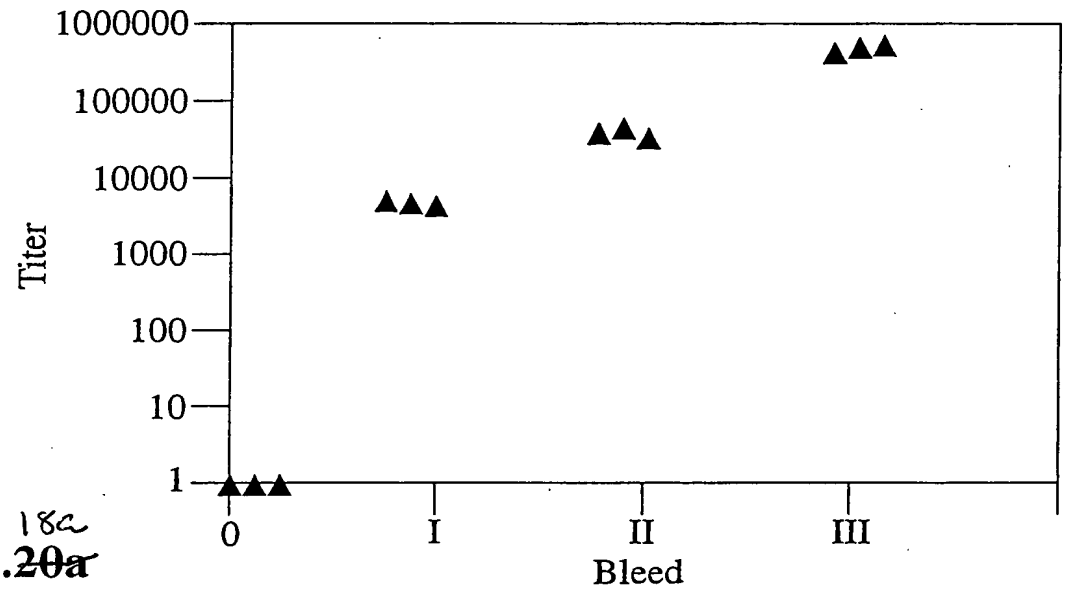


Fig 16d ~~18d~~

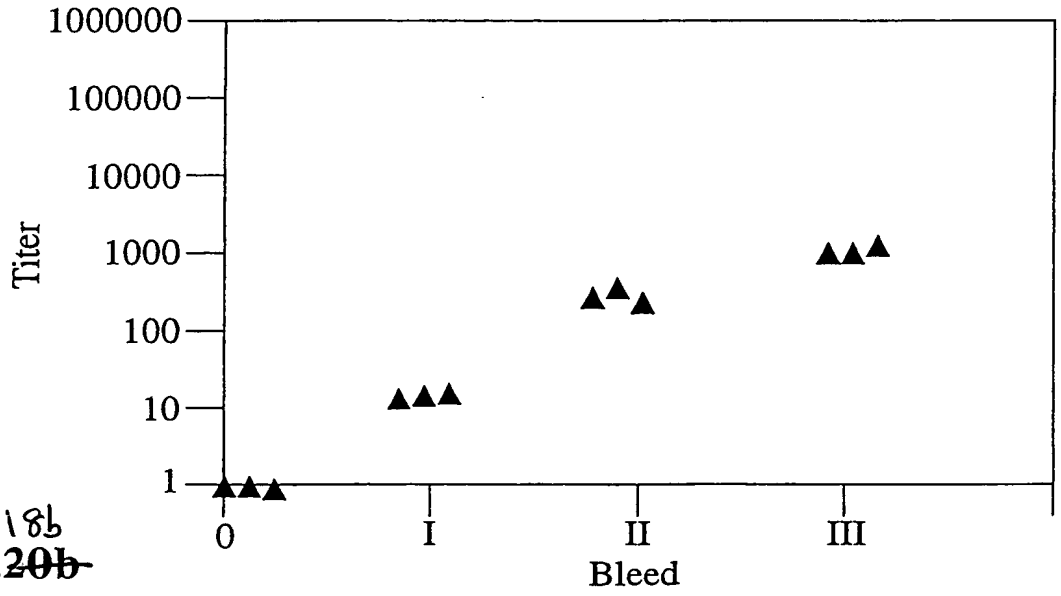




17
FIG.~~19~~



18a
FIG.~~20a~~



18b
FIG.~~20b~~

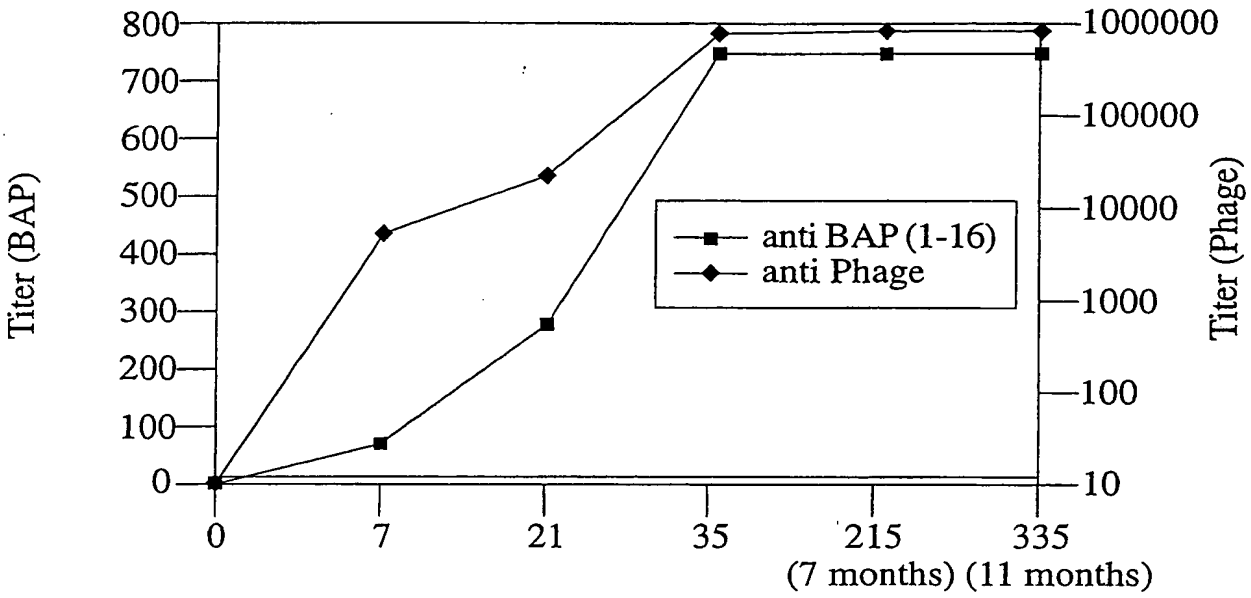


FIG. ~~21~~ 19

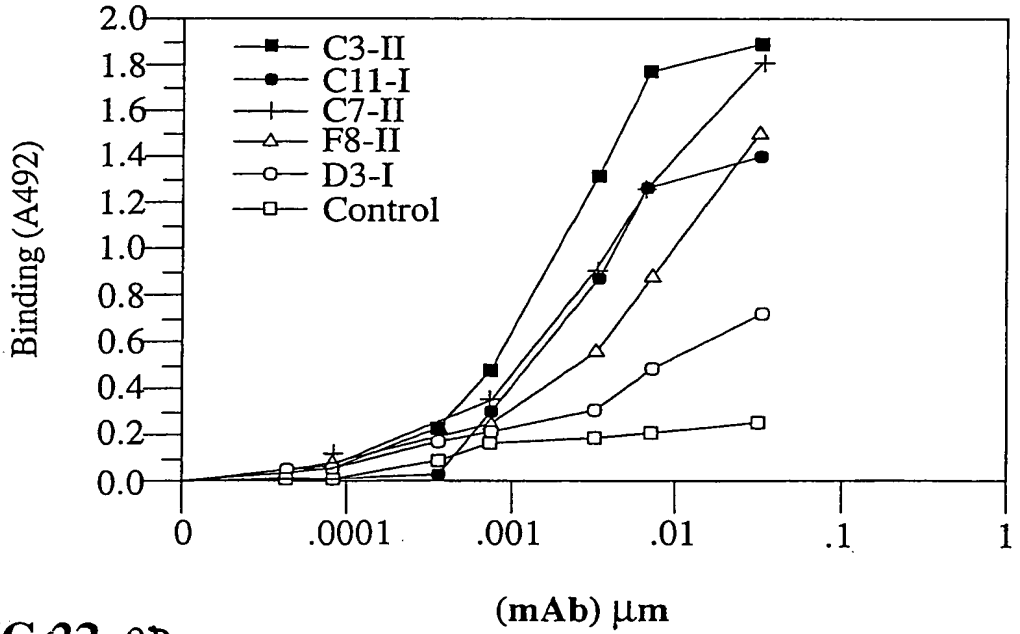


FIG. ~~22~~ 20

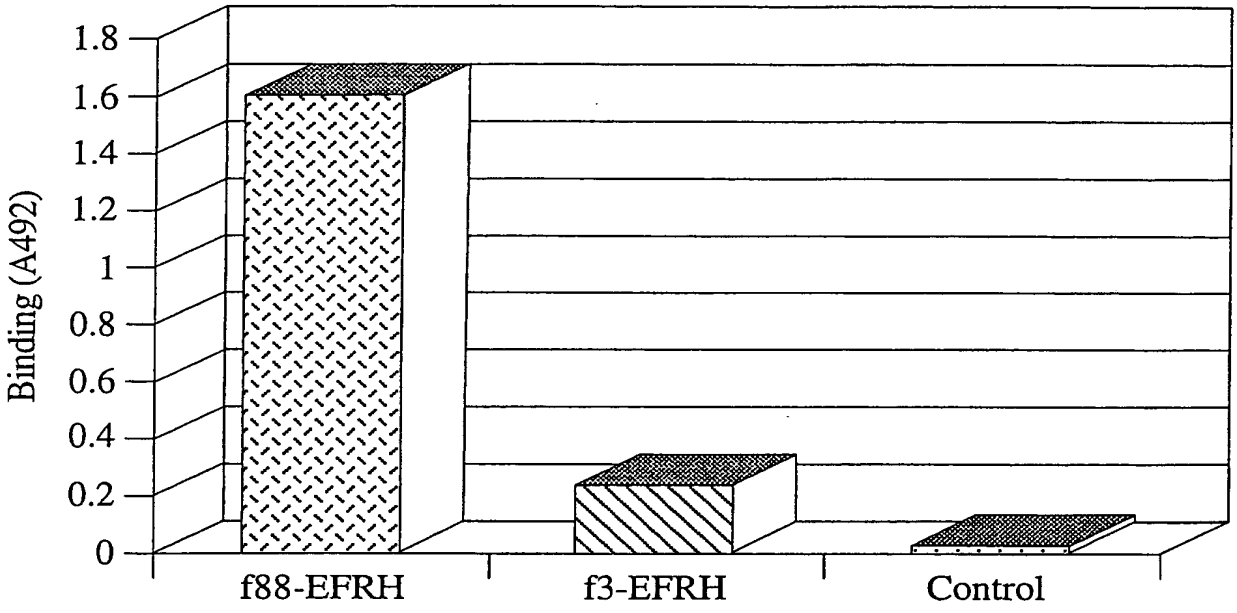


FIG.~~23~~ 21

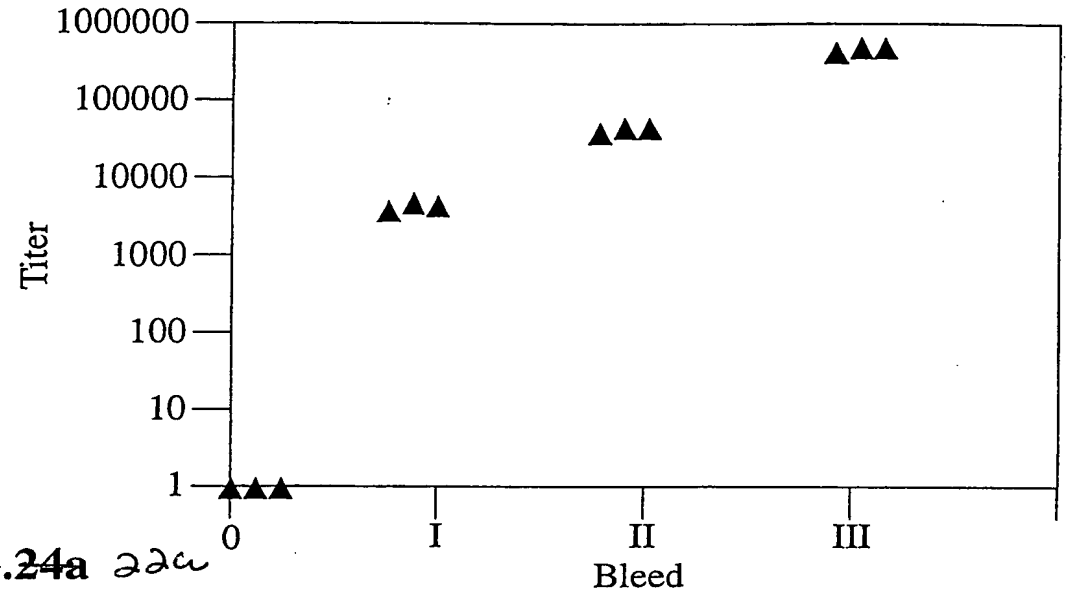


FIG.~~24a~~ 22a

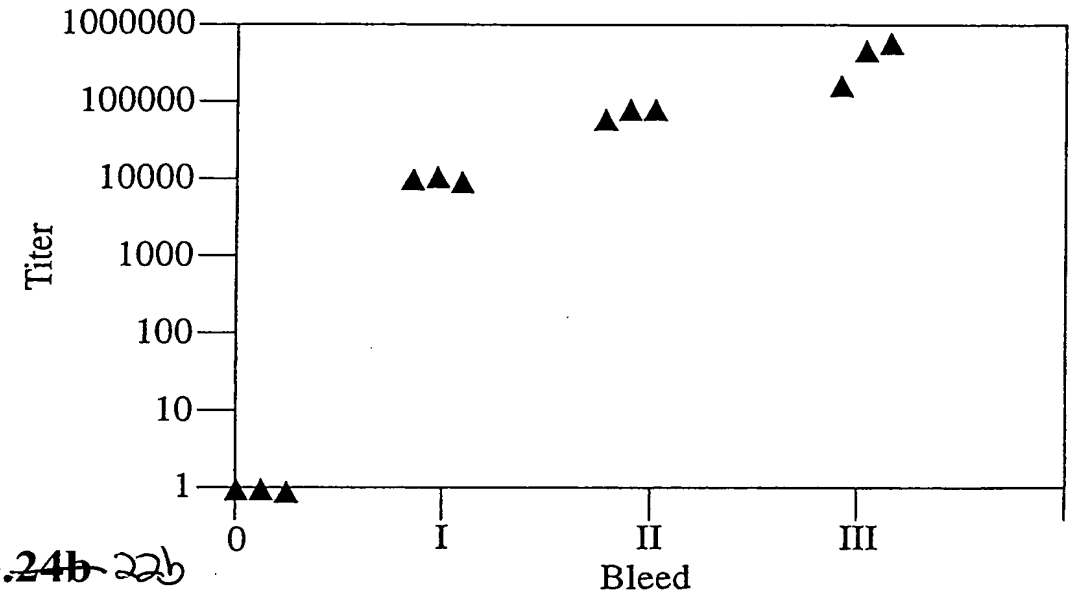


FIG.~~24b~~ 22b

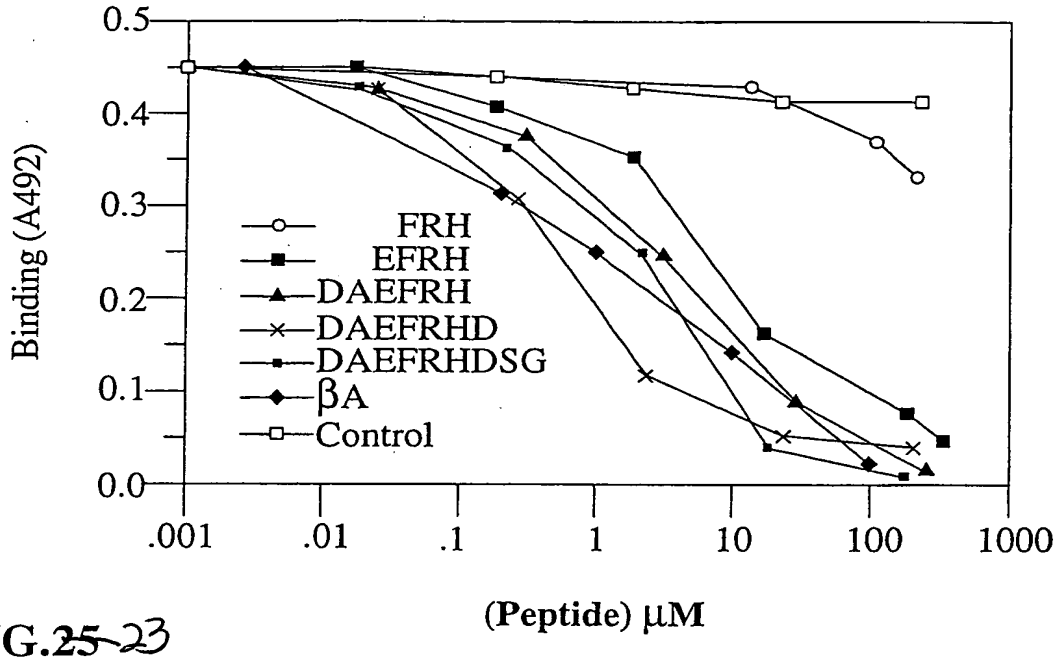


FIG.~~25~~ 23

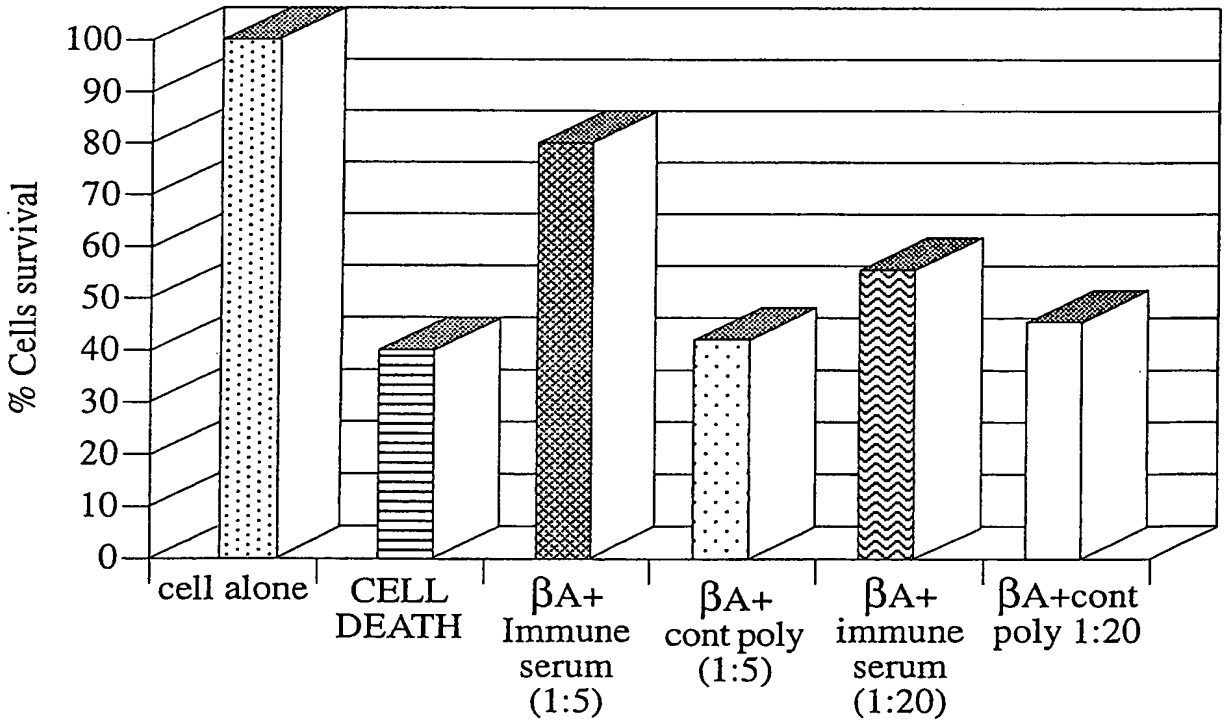


FIG.~~26~~ 24

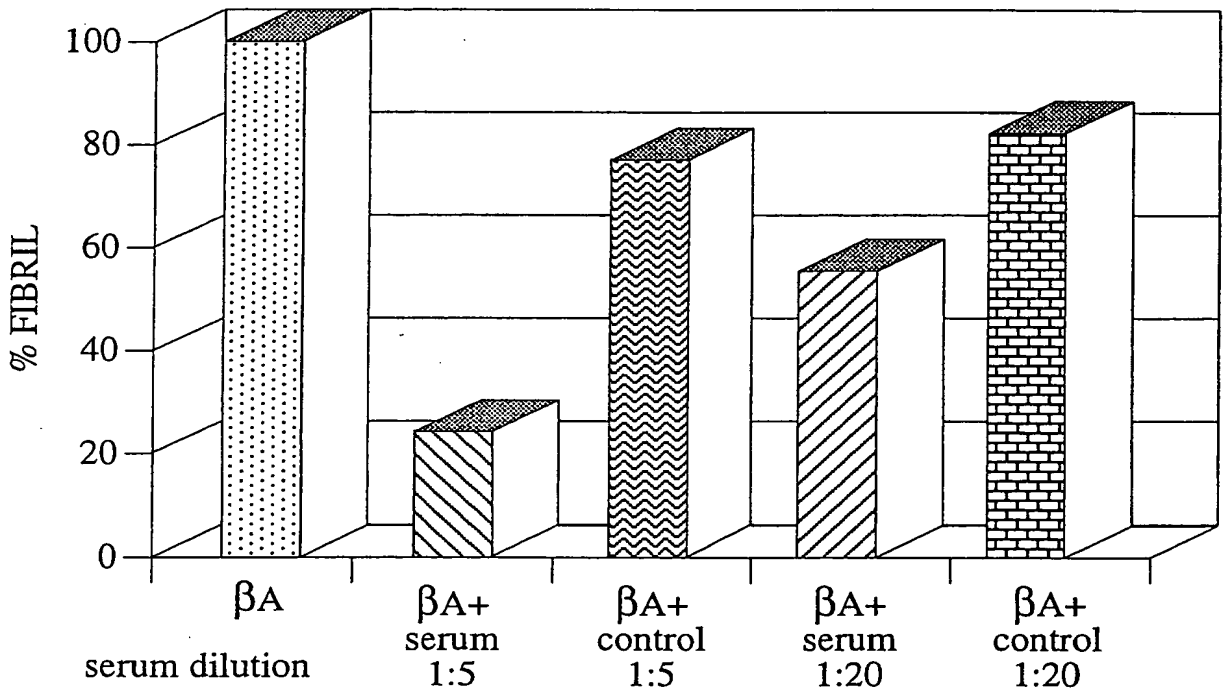


FIG.~~27~~ 25

Human	PrP 106-126:	KTNMKHMAGAAAAGAVVGGLG
Mouse	PrP 105-125:	KTNLKHVAGAAAAGAVVGGLG

FIG.28 24

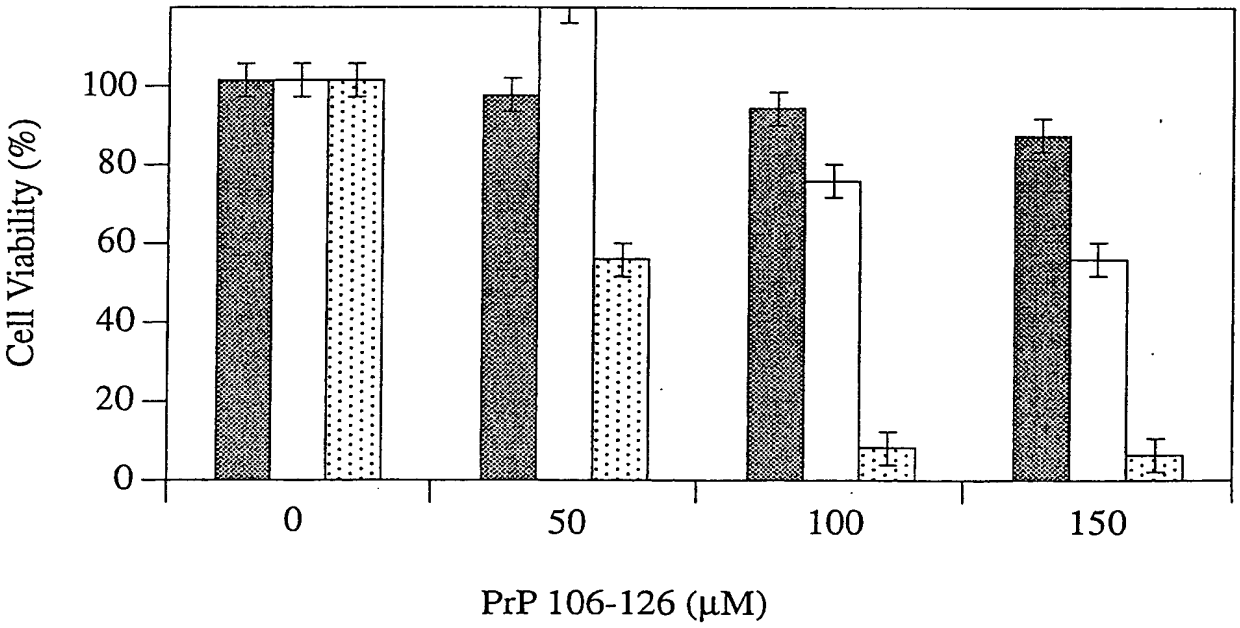


FIG.29 27

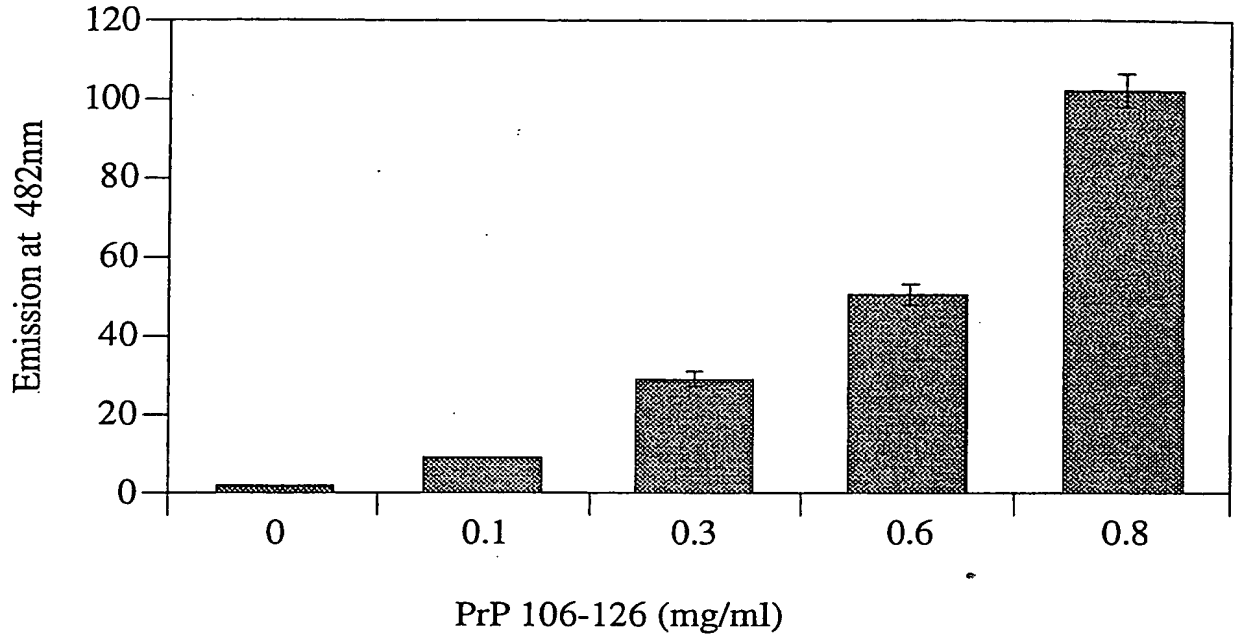


FIG.~~30~~ 28

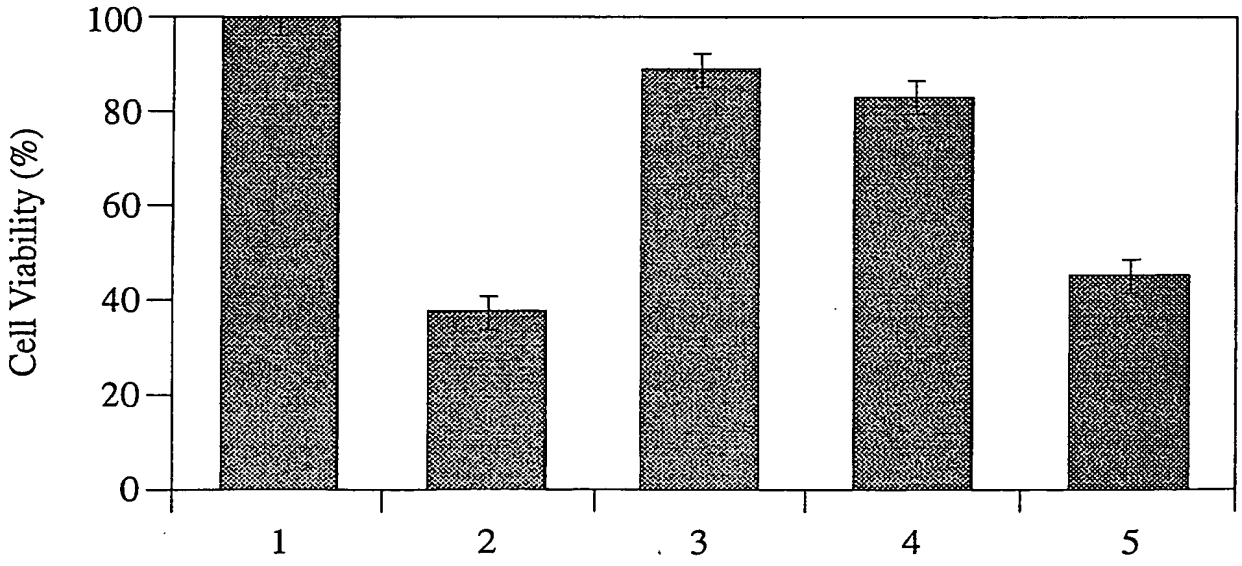


FIG.~~31~~ 29

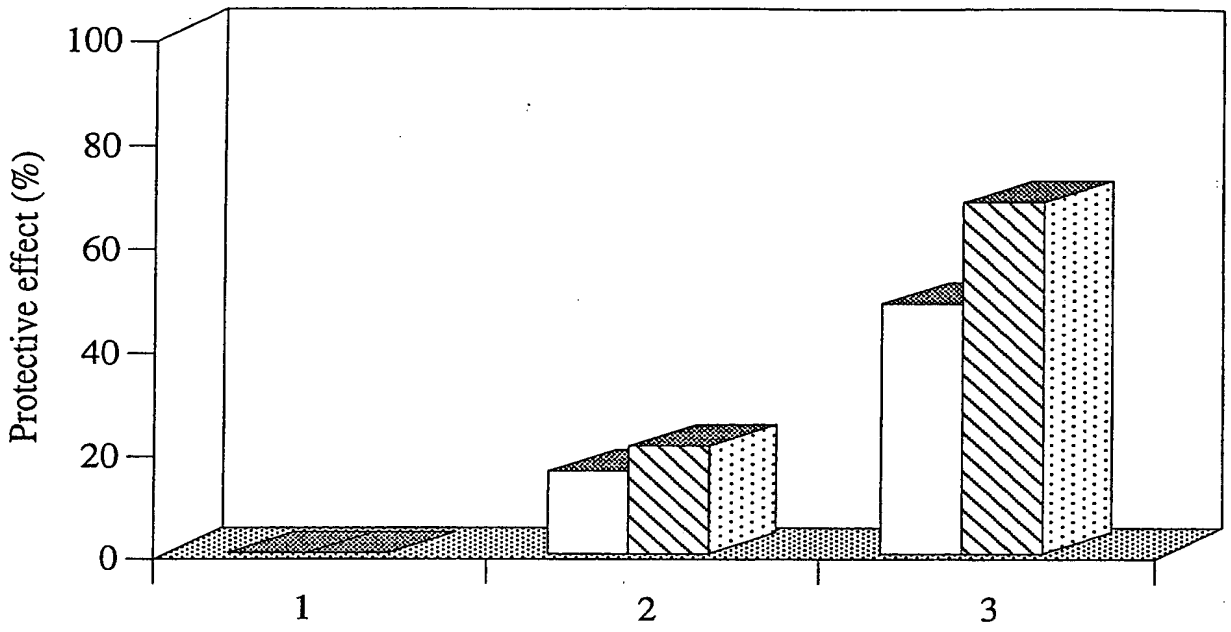


FIG.~~32~~ 30

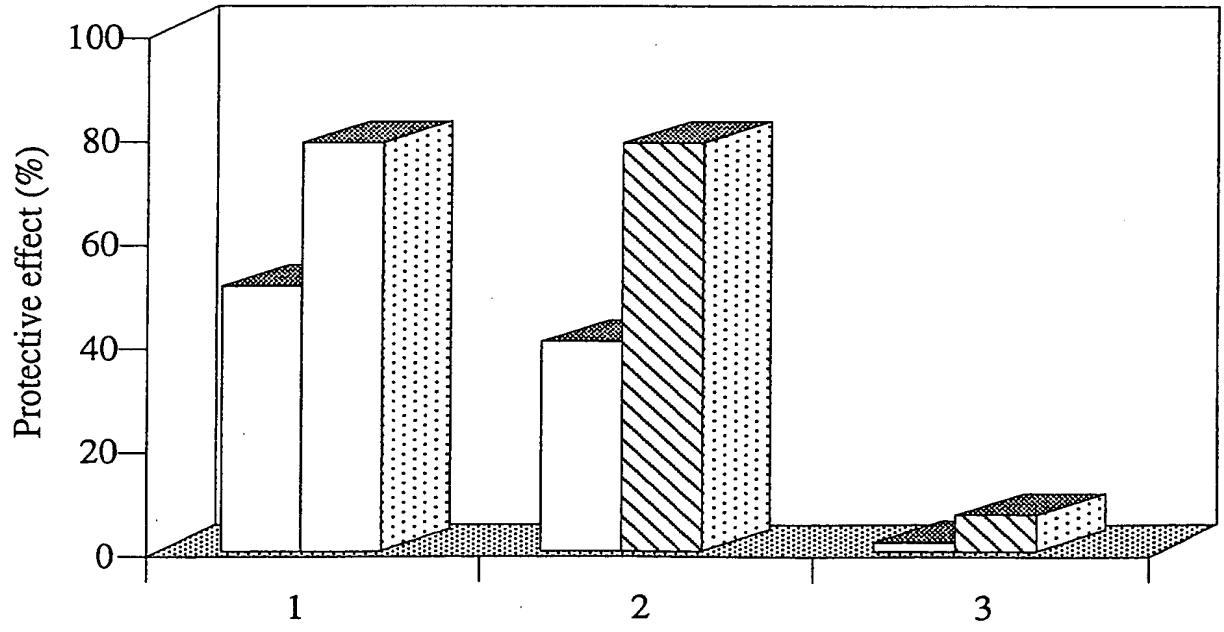


FIG.~~33~~ 31